

(FILE 'HOME' ENTERED AT 10:59:24 ON 14 MAR 2003)

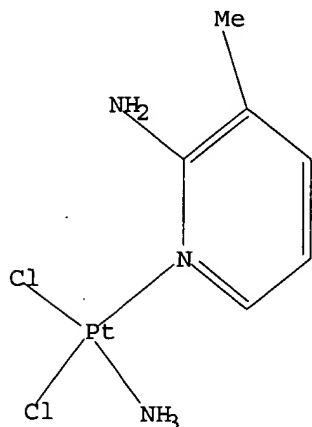
FILE 'REGISTRY' ENTERED AT 11:00:13 ON 14 MAR 2003

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 11:00:40 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 11:00:50 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

100.0% PROCESSED 20 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 11:00:55 ON 14 MAR 2003

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FILE COVERS 1907 - 14 Mar 2003 VOL 138 ISS 12
FILE LAST UPDATED: 13 Mar 2003 (20030313/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 1 L3

=> d bib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 2000:889230 CAPLUS

DN 134:202420

TI High-throughput synthesis and screening of platinum drug candidates

AU Ziegler, Christopher J.; Silverman, Adam P.; Lippard, Stephen J.

CS Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

SO JBIC, Journal of Biological Inorganic Chemistry (2000), 5(6), 774-783
CODEN: JJBCFA; ISSN: 0949-8257

PB Springer-Verlag

DT Journal

LA English

OS CASREACT 134:202420

AB Platinum drugs play an important role in the treatment of cancer, but there is room for improvement. Here we present a new platinum drug-discovery strategy to identify compds. having efficacy equiv. to that of cisplatin with the expectation that some may increase the spectrum of treatable tumors and/or reduce dose-limiting toxicity. Platinum drug candidates were generated through the use of automated synthesis, taking advantage either of the trans effect or by using silver chloride pptn. to activate the starting materials. Reaction products were screened for activity in a high-throughput transcription assay and the most promising candidates characterized. Over 3600 reaction products were screened for their ability to inhibit transcription of .beta.-lactamase in the BlaM HeLa cell line by monitoring cleavage of a lactam ring linking the two halves of a fluorescent resonance energy transfer (FRET) dye, CCF2/AM. From this screen, three reactions produced good candidates, and four species were identified among these reaction products. Three of the compds., cis-[(isopropylamine)2PtCl2], cis-[(cyclobutylamine)2PtCl2], and cis-[ammine(cyclobutylamine)PtCl2], have been previously detd. to be active cisplatin analogs. The fourth compd., cis-[ammine(2-amino-3-picoline)PtCl2], represents a new kind of antitumor drug candidate similar to ZD0473, a recently reported analog. The discovery of these compds. represents an important proof of principle that platinum anticancer drug candidates can be rapidly prepd. and screened in this manner.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

(FILE 'HOME' ENTERED AT 11:11:06 ON 14 MAR 2003)

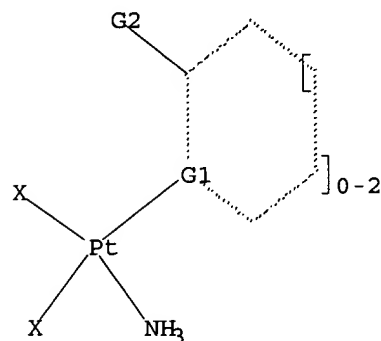
FILE 'REGISTRY' ENTERED AT 11:11:39 ON 14 MAR 2003

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 S,N,P

G2 OH,SH,MeO,EtO,NH2

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 11:12:07 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 864 TO ITERATE

100.0% PROCESSED 864 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 15517 TO 19043

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1full

L3 0 L1FULL

=> s l1 full

FULL SEARCH INITIATED 11:12:22 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 17375 TO ITERATE

100.0% PROCESSED 17375 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

L4 1 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

152.77

152.98

FILE 'CAPLUS' ENTERED AT 11:12:35 ON 14 MAR 2003

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FILE COVERS 1907 - 14 Mar 2003 VOL 138 ISS 12
FILE LAST UPDATED: 13 Mar 2003 (20030313/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4
L5 1 L4

=> d bib abs

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2000:889230 CAPLUS
DN 134:202420
TI High-throughput synthesis and screening of platinum drug candidates
AU Ziegler, Christopher J.; Silverman, Adam P.; Lippard, Stephen J.
CS Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SO JBIC, Journal of Biological Inorganic Chemistry (2000), 5(6), 774-783
CODEN: JJBCFA; ISSN: 0949-8257
PB Springer-Verlag
DT Journal
LA English
OS CASREACT 134:202420
AB Platinum drugs play an important role in the treatment of cancer, but there is room for improvement. Here we present a new platinum drug-discovery strategy to identify compds. having efficacy equiv. to that of cisplatin with the expectation that some may increase the spectrum of treatable tumors and/or reduce dose-limiting toxicity. Platinum drug candidates were generated through the use of automated synthesis, taking advantage either of the trans effect or by using silver chloride pptn. to activate the starting materials. Reaction products were screened for activity in a high-throughput transcription assay and the most promising candidates characterized. Over 3600 reaction products were screened for their ability to inhibit transcription of .beta.-lactamase in the BlaM HeLa cell line by monitoring cleavage of a lactam ring linking the two halves of a fluorescent resonance energy transfer (FRET) dye, CCF2/AM. From this screen, three reactions produced good candidates, and four species were identified among these reaction products. Three of the compds., cis-[(isopropylamine)2PtCl2], cis-[(cyclobutylamine)2PtCl2], and cis-[ammine(cyclobutylamine)PtCl2], have been previously detd. to be active cisplatin analogs. The fourth compd., cis-[ammine(2-amino-3-picoline)PtCl2], represents a new kind of antitumor drug candidate similar to ZD0473, a recently reported analog. The discovery of these compds. represents an important proof of principle that platinum anticancer drug candidates can be rapidly prepd. and screened in this manner.
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ALL CITATIONS AVAILABLE IN THE RE FORMAT